REMARKS

This is in response to the Office Action dated October 15, 2010. Claims 1-9 are pending. Claim 8 is amended to add Markush language. Thus, this amendment is formal in nature and does not change the scope of the claim. No claims are added or deleted. Thus, with the entry of this response, claims 1-9 will remain active. No new matter is added with the amendment.

I. Rejections under 35 USC § 103

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Suh, WO 03/007947 publication ("Suh"), in view of Karsenty et al., WO 01/53477 publication ("Karsenty"), and further in view of Allen et al., US Patent No. 5,914,329 ("Allen") (all of previous record). Applicants respectfully traverse this rejection.

Applicants have previously asserted that Karsenty and Allen are not relevant to the claimed invention because these references concern a chemical compound that is unrelated to the compound of the invention and that the chemical arts are unpredictable. That is, in the chemical arts, what works with one compound may not work for another; and therefore, one of skill in the art would not extrapolate from the combined teachings of Karsenty and Allen to arrive at the presently claimed invention, in view of Suh. Applicants believe this position is legally sound and maintain that position here.

However, applicants further point out that the Examiner's arguments are based upon a misinterpretation or overly broad reading of Karsenty and Allen. The Examiner's position appears to be that Karsenty and Allen suggest that the di-mesylate salts of **all** active agents are preferred over other salts. In particular, the Examiner has indicated that: "Karsenty et al. and Allen et al. teach that the dimesylate salts of other active agents are preferred over other pharmaceutical salts ..." (Office Action at page 3, lines 4-5) and "Therefore, as Allen et al. teaches that the dimesylate salts have improved solubility, stability and bioavailability over other salts" (Office Action at page 3, lines 6-8). Applicants are of the opinion that the Examiner's perspective, as shown by these

quotations, is defective in concluding that Karsenty and Allen suggest dimesylate salts of compounds are better in all instances.

First, with regard to Karsenty's teachings, the Examiner appears to read more into Karsenty than is actually there. Dimesylate salts are described in Karsenty at page 57-58, as follows:

Similarly, numerous NPY-R, antagonists have been identified. Examples of such antagonists include, but are not limited to α-alkoxy and α-thioalkoxyamide compositions (*See, e.g.*, U.S. Patent No. 5,939,462); dihydropyridine based compounds (*See, e.g.* U.S. Patent Nos. 5,554,621, 6,001,836, 5,668,151, and 5,635,503); substituted benzylamine derivatives (*See, e.g.*, U.S. Patent Nos. 5,985,873, 5,962,455 and 5,900,415); dihydropyrimidone derivatives (*See, e.g.*, U.S. Patent No. 5,889,016); naphthimidazolyl derivatives (*See, e.g.*, U.S. Patent No. 5,776,931): dimesylate salts (*See, e.g.* U.S. Patent No. 5,914,329) and substituted benzofurans, benzothiophenes or indoles (*See, e.g.* U.S. Patent No. 5,663,192). Additional NPY-R antagonists are disclosed in U.S. Patent Nos. 5,567,714, 5,504,094, 5,670,482, 5,989,920, 5,827,853 and 5,985,616.

As described above, Karsenty simply mentions dimesylate salts as one of numerous NPY-R antagonists. Further, Karsenty describes dimesylate salts by referring to U.S. Patent No. 5, 914,329. In fact, Karsenty teaches that NPY-R antagonists could be used in the form of a dimesylate salt in one specific compound (which is not **all** active agents but is the compound disclosed in U.S. Patent No. 5,914,329 **only**). Thus, Karsenty does not teach or suggest that the dimesylate salts of other active agent are preferred over other pharmaceutical salts.

With regard to Allen, dimesylate salts are described in column 3, lines 46-58, as follows:

Previously known salts of cis-1-(3-ethoxyphenyl)-1-(4-phenylpiperazin-1-yl)-4-methyl-cyclohexane have been found to be insoluble and/or of poor chemical stability. For example, the fumarate salt has low solubility (40 µg/ml) in water and low bioavailability in dogs (2%-18%). The dihydrochloride has good water solubility (1 mg/ml) and bioavailability in dogs (75%), but was found to be unstable in the solid state.

We have found that the dimesylate salt (compound 1) has a solubility of 31 mg/ml, good stability and bioavailability; these superior properties make it useful for pharmaceutical applications.

Applicants first point out that Allen is U.S. Patent No. 5, 914,329, the very patent that Karsenty refers to above. And, as applicants have asserted above, Allen simply describes that the dimesylate salt of cis-1-(3-ethoxyphenyl)-1(4-(phenylpiperazin-1-yl)-4-methyl-cyclohexane only (not all active agents) is preferred. Further, Allen does not describe any other active agents.except cis-1-(3-ethoxyphenyl)-1-(4-phenylpiperazin-1-yl)-4-methyl-cyclohexane. Thus, Allen does not teach or suggest that the di-mesylate salts of **other** active agents are preferred over other pharmaceutical salts.

As can be readily seen from the above, Karsenty and Allen do not teach or suggest that the di-mesylate salts of **all** active agents are preferred over other salts.

Further, applicants assert that the Examiner's opinion is based on the assumption that Suh, Karsenty and Allen could be combined because they all are related to "the treatment of osteoporosis." In particular, the Examiner indicated that "the di-mesylate salt of the active agent taught by Allen et al. is also used to treat osteoporosis." (Office Action at page 4, line 1-2).

However, applicants point out that the present invention is related to a pharmaceutical salt of 2 methanesulfonic acid. The formation of a salt is a reaction of acid and base so, it is important to identify whether the compound of the active agent is basic or acidic. If it is basic, the pharmaceutical salt should be acid, and vice versa.

It is noted that there are other active agents for the "treatment of osteoporosis" such as Boniva® (ibandronate sodium); (*see* http://en.wikipedia.org/wiki/ibandronate) and Actonel® (risedronate sodium); (see http://en.wikipedia.org/wiki/ Actonel). Such compounds are acidic compounds so their salts should be basic such as a sodium salt. A methanesulfonic acid salt like those described in Allen could not be prepared with such osteoporosis treating compounds.

The determination of whether the compound of an active agent is basic or acidic is closely related to chemical structure. Thus, in preparing a pharmaceutical salt of an

active agent, one skilled in the art should consider not the activity (such as "to treat osteoporosis") but the chemical structure of the active agent.

Karsenty and Allen describe only cis-1-(3-ethoxyphenyl)-1-(4-phenylpiperazin-1-yl)-4-methyl-cyclohexane, which is completely different from the present invention in chemical structure, so Karsenty and Allen could not be combined with Suh when preparing salts.

In conclusion, applicants assert that (1) the Examiner has misread the prior art, in that Karsenty does not teach or suggest that di-mesylate salts of other active agents are preferred over other pharmaceutical salts, and (2) the Examiner's assumption, that Suh, Karsenty and Allen could be combined because each is related to the treatment of osteoporosis, is unreasonable. As previously pointed out, one of skill in the art would not have considered a structurally unrelated compound, like the chemical compound of Karsenty and Allen, to guide them in modifying the compound of Suh.

In view of these remarks, applicants respectfully request the Examiner to carefully review the cited art and these arguments and to withdraw this rejection under 35 USC § 103.

II. Double Patenting Rejections

Claims 1 and 3-9 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 14-20 of copending Application no. 11/577,469. This rejection has been modified from the previous rejection presented in the office action dated 4/14/2010, due to the cancellation and addition of new claims in the co-pending application. In response, applicants herewith file a Terminal Disclaimer.

Claims 1-9 are rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-3, 5-8, 9-11, and 13-15 of U.S. Patent No. 7,662,840. Applicants respectfully traverse this rejection for all of the reasons set forth above and in previous responses in connection with the pending rejections under 35 USC § 103 rejections. Withdrawal of this rejection is respectfully requested.

III. Terminal Disclaimer

The Terminal Disclaimer filed on 8/10/2010 was alleged to be improper, as it refers to 35 USC § 154, 156 and 173; 35 USC § 155 and 156, which do not define the term of the patent. The Terminal Disclaimer has not been accepted. In response, applicants herewith submit a revised Terminal Disclaimer.

CONCLUSION

In view of the above arguments and the attached Terminal Disclaimer, applicants respectfully request the Examiner to reconsider and withdraw all outstanding rejections. A Notice of Allowance is respectfully requested. The Examiner is invited to contact the undersigned attorney for applicant for any reason related to the advancement of this case.

In the event that additional fees are necessary in view of this amendment then such fees are hereby authorized to be charged to our Deposit Account No. 01-2300 referencing docket number 027707.00031.

Respectfully submitted,

February 4, 2011

Patricia D. Granados

Patricia D. Granados
Registration No. 33,683

Customer No. 004372
ARENT FOX LLP
1050 Connecticut Avenue, N.W.,
Suite 400
Washington, D.C. 20036-5339
Tel: (202) 857-6000
Fax: (202) 638-4810
PDG/ars